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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/747,524	12/19/2000	Y. Tom Tang	PC-0022 CIP	9999

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INCYTE GENOMICS, INC.
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER	
HILL, MYRON G	

ART UNIT	PAPER NUMBER
1648	13

DATE MAILED: 01/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/747,524	TANG ET AL.	
	Examiner	Art Unit	
	Myron G. Hill	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *27 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1- 20* is/are pending in the application.

4a) Of the above claim(s) *7- 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1- 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This office action is in response to Amendment B, paper 11, filed 9/27/02.

Claims 1- 6 are under consideration in this office action. The 1.132 Declaration of Michael Walker has been considered and is discussed below.

Response to Amendment

REJECTIONS WITHDRAWN

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1- 6 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is withdrawn because it is moot in light of the amendment.

REJECTIONS MAINTAINED

Claim Rejections - 35 USC § 112

Claims 1- 6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. Applicant discloses that the DNA and

protein are useful in the diagnosis and treatment of disorders associated with inflammation (page 3, lines 7- 9).

The rejection concluded as follows:

Considering the long list of possible diseases, drawn to many different populations having conditions with different symptoms and disease endpoints, the amount of work needed to establish the association/ correlation of a particular disease state, the very general nature of the teachings in the specification, and the lack of working examples that show the ability to specifically diagnosis a specific condition or treat a condition in a specific way, it is considered to require undue experimentation to use the invention.

Applicant submits the following arguments:

That the invention meets the utility requirement of 101 and 112, that there is homology between the claimed sequence and KIM which is "described as associated with kidney injury" and "KIM may be an inflammation protein specifically associated with kidney", that one skilled in the art would recognize the value of diagnosis and treatment of inflammation while further tests are underway to determine the underlying condition, that Figure 3B lists all 159 cDNA libraries where the sequence of GRIIP was found, and the declaration of Dr. Walker where he asserts that "when used in a tissue specific and clinically relevant manner, GRIIP expression is diagnostic of cancers of the bone or spleen."

In the declaration of Dr Walker, paragraph section 4 which starts to discuss the invention, he repeats a quotation of the specification asserts the usefulness of the sequence but this does not illustrate anything more than what was disclosed in the specification. Also, the last sentence deals with differential

expression and it is not clear that this is shown in Figures 3A and 3B. Paragraph section 5 of the declaration continues with discussion of the libraries where the sequence was found and concludes with the statement that an independent report associates GRIIP with bone marrow cancer.

The arguments have been fully considered and not found persuasive.

First, the examiner is not rejecting the possible utility of the sequence but the burden of experimentation needed to make a specific diagnostic test. The assertion that this sequence has homology to another protein that is associated with kidney does not mean that this sequence will have the same association. The fact that the sequence is found in cDNA libraries does not prove a specific relationship/ association with a particular disease state. Applicant has not shown that this sequence can be a diagnostic test of an individual or used in testing a defined population of people who are to be screened for cancers.

The art has not established that the expression of an mRNA in a cDNA library would allow any one to conclude that it is a diagnostic marker for the disease. Contrary to Applicants argument, the determination of a cancer marker must be based on studying results from a considerable number of patients, and statistical analysis. For instance, the Guidelines for Marker Development by the National Cancer Institute (NCI) clearly indicate the data required to proceed, and the considerations for preliminary identification of a potentially useful marker in the initial step. Some of the considerations in the Guidelines are:

"Step 1: ... Can a patient *population* be defined for which this marker may have utility? What is an expected range for the

prevalence of this marker in population of potential interest? ....
The number of specimens that should be assessed at this stage will vary depending on the question asked or the intended use of the marker. If *prevalence is being assessed*, then >20 specimens should be examined so that a marker present in 5% of cases would have a reasonable chance of being detected in the set of specimens. The numbers to be assessed for other questions will depend on the statistical design, the difference that would be meaningful to detect. .... Estimate prevalence of the marker on an *expanded* collection of targeted specimens.
Step 5: ... The intended use should be more clearly defined and careful *statistical* designs applied to studies that usually have to include *large number of cases*."

For the obvious reason, none of the critical questions or considerations for the determination of a cancer marker above can be answered or met by the present application.

In Figure 3A, there are other categories of libraries that have a higher percent of cDNA detection (column 3) and other categories that have a higher percent abundance (column 5). There are positive cDNA findings in almost all the other groups of clone libraries.

The specification asserts a usefulness as a diagnostic but there is no showing that a specific diagnostic is possible. Applicant argues that the

sequence is associated with inflammation, and bone or spleen cancers, but Applicant has not taught "tissue specific and clinically relevant manner" in which it can be used. There is no showing that when this sequence is detected in a organism, there is a correlation with a particular disease state or condition.

Therefore, the asserted use for diagnosis cancer is not credible and the rejection of record is maintained because it would require undue experimentation to use the invention.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 703-308-4521. The examiner can normally be reached on 9am-6pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4247. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Myron G. Hill
Patent Examiner
December 27, 2002

JAMES HOUSEL 12/30/02
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600